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Original Article

The Incidence and Risk Factors of Acute Asymptomatic Brain Infarcts After Percutaneous Coronary Intervention in Patients with Acute Myocardial Infarction☆

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SUMMARY

Objective: This study aimed to evaluate the incidence and related factors of acute asymptomatic brain infarcts (aABI) following percutaneous coronary intervention (PCI) in patients with acute myocardial infarction (AMI) via the right radial approach.

Patients and methods: Two hundred ten consecutive patients with AMI were enrolled. Multiple factors were compared between patients with (n = 37) and without (n = 138) aABI in 175 patients who underwent PCI.

Results: Of 175 patients with AMI, 37 (21.14%) developed aABI as determined by diffusion-weighted magnetic resonance imaging (MRI). Incidence of hypertension, proportion of primary PCI (p-PCI), Killip > 1 on admission, duration of procedure, and the frequency of device insertion into the coronary artery significantly differed between the aABI and non-aABI groups. These significant factors were reevaluated using logistic regression. Proportion of p-PCI, duration of the procedure, and the frequency of device insertion into the coronary artery were indicated as independent factors related to the incidence of aABI and others did not.

Conclusion: Cranial MRI imaging following PCI revealed that 21.14% of the patients with AMI had aABI. The independent factors related to aABI following PCI were p-PCI, duration of the procedure, and the frequency of device insertion into the coronary artery.

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1. Introduction

For patients with acute myocardial infarction (AMI), percutaneous coronary intervention (PCI) is one of the most effective ways of maintaining cardiac function and decreasing mortality. Following equipment and technology development in PCI, the transradial intervention (TRI) is enlarged, especially in China. However, cardiac intervention is also a recognized cause of the serious complication of symptomatic acute ischemic stroke (sAIS), although the incidence is rare (0.11–0.38%)[1–5]. Recent advances in magnetic resonance imaging (MRI), such as diffusion-weighted imaging (DWI), have detected small and hyperacute lesions of ischemic stroke, even in patients without clinical symptoms. A previous study showed that the incidence of acute asymptomatic brain infarcts (aABI) was in 11% of patients undergoing elective coronary angiography and in 23% of those having elective PCI (e-PCI)[6]. Another study reported that patients with acute coronary syndrome (ACS) undergoing primary PC I(p-PCI) the incidence of asymptomatic acute ischemic stroke reached 34.7%[7]. The incidence and risk factors of aABI in patients with AMI after PCI through TRI were rarely reported. The current study assessed the incidence and related factors of aABI following PCI in patients with AMI.

☆ Conflicts of interest: The authors declare that they have no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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2. Patients and methods

2.1. Study design and study participants

We prospectively studied 210 patients with AMI in two large hospitals (Beijing Anzhen Hospital, Beijing Daxing Hospital) and Capital Medical University in Beijing. The inclusion period was February 2011 to October 2011. Our study included 175 consecutive patients with PCI through a right radial approach (study group), Of these patients, 118 were ST-segment elevation myocardial infarction (STEMI; 76 patients were treated by P-PCI, 24 patients were treated with thrombolytic therapy and e-PCI, 18 patients were treated with conservative therapy, and e-PCI) and 57 patients were non-ST segment elevation myocardial infarction (NSTEMI; 9 patients were treated with P-PCI, 48 patients were treated with conservative therapy and e-PCI). The study protocol was approved by the Medical Ethics Committee of Beijing Anzhen Hospital, Beijing Friendship Hospital, Beijing Daxing Hospital, and Capital Medical University (Fig. 1).

The control group was defined as 35 consecutive patients with AMI but without PCI because of any causes that could not complete coronary angiography. Of these, 14 patients with STEMI treated with thrombolytic therapy refused e-PCI, and 21 patients undergoing conservative treatment were unable to give informed consent.

All participants provided written informed consent to cranial MRI (Avanto 1.5T, SIEMENS, Germany), including FLAIR, DWI, T2- and T1-weighted MRI, and magnetic resonance angiography (MRA). The control group underwent these procedures within a mean of 2.0 ± 1.0 days after admission, and the study group underwent these procedures within a mean of 3.0 ± 1.0 days after PCI. Lesions that generated high intensity with a low apparent diffusion coefficient value on DWI were considered to be aABI[8]. Patients in the study group were assigned to subgroups based on the presence or absence of aABI. Cranial MRIs were interpreted by two radiologists who specialize in cerebral imaging and were unaware of the subgroup sequencing of the patients. We recorded the following factors: age, body mass index, (BMI) sex, coronary risk factors (smoking, hyperlipidemia, diabetes mellitus, and hypertension), ≥50% stenosis in the extracranial carotid arteries on MRA, and laboratory data.

2.2. Study definitions and catheter procedure

The diagnosis of AMI is defined as a clinical (or pathologic) event caused by myocardial ischemia in which there is evidence of myocardial injury or necrosis. Criteria are met when there is an increase and/decrease in cardiac biomarkers, along with supportive evidence in the form of typical symptoms, suggestive electrocardiographic changes, or imaging evidence of new loss of viable myocardium or new regional wall motion abnormality[9,10].

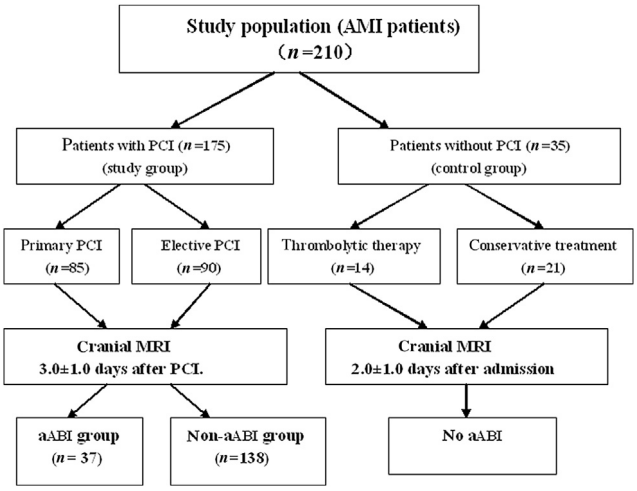

Fig. 1. Distribution of the population groups in the study.

Five cardiologists randomly performed PCI after admission. After oral administration of the loading dose of 300 mg of aspirin and 600 mg of clopidogrel, the routine maintaining dose of 100 mg of aspirin and 75 mg of clopidogrel was administered. The 175 consecutive patients underwent p-PCI and e-PCI through the right radial artery using a 6 French guiding catheter. Only the cobalt-chromium alloy, coronary RESOLUTE stent (Medtronic Inc, Minneapolis, MN, USA), was implanted according to operator discretion because of its nonferromagnetic properties. After a sheath was inserted, 5000 U of unfractionated heparin was administered and another 5,000 U were added before the initiation of e-PCI and p-PCI.

2.3. Exclusion criteria

Patients were excluded if they had contraindications to MRI, such as out-of-hospital cardiac arrest or circulatory support including intra-aortic counterpulsation or percutaneous cardiopulmonary support, history of cerebral ischemia (stroke or transient ischemic attack within the past 3 months), atrial fibrillations, valvular heart disease, congestive heart failure with low ejection fraction, unstable vital parameters, and pregnancy. Because TRI is in common use, during the period of our study, only four patients with right femoral approach and two patients with left radial approach were excluded.

2.4. Statistical analysis

Categorical data were presented as frequencies (percentages); continuous data were presented as mean value ± standard deviation. Continuous variables were compared between the two groups using the Mann-Whitney *U* test. Demographic variables for categorical data were compared using the chi-square or Fisher exact test where appropriate. Statistically significant factors were examined using multivariate logistic regression. A p value < 0.05 (two-sided) was considered significant. Data were analyzed with SPSS 21.0 software (IBM, Chicago, IL).

3. Results

Cranial MRI was safely accomplished in all patients. None of the control patients had aABI, whereas 37 in the study group had aABI (0% vs. 21.14%, $p = 0.006$). No one in the study population had sAIS. All aABI lesions were round in shape and their diameter was 1 cm or less on DWI. In the study group, the incidence of aABI was 21.14%. As shown in Table 1, the aABI and non-aABI groups comprised 37 and 138 patients, respectively. The incidence of hypertension and p-PCI significantly differed between the aABI and non-aABI groups, whereas age, BMI, sex, incidence of hyperlipidemia and diabetes mellitus, STEMI, and prevalence of extracranial carotid artery stenosis did not. We recorded the laboratory data on admission (Table 2). There were no significant differences in the laboratory data on admission among patients with aABI and those without aABI. We used some biochemical indicators to assess the severity of AMI (Table 3), maximum creatine kinase isoenzyme MB (CK-MB) mass, cardiac troponin-I (cTnI) and B-type natriuretic peptide values were not statistically significant. The patients with aABI experienced a higher rate of Killip classification (>1) on admission. Table 4 outlines the results of angiography characters and catheter procedure. Patients with aABI experienced greater duration of

Table 1
Characteristics of the study group.

	aABI group	Non-aABI group	*p*
	$n = 37$	$n = 138$	
Age	58.0 ± 8.4	60.1 ± 10.1	0.247
Male	23 (62.2%)	98 (71%)	0.301
BMI (kg/m^2)	25.2 ± 4.7	24.9 ± 4.5	0.722
Smoking	16 (43.2%)	75 (54.3%)	0.230
Hyperlipidemia	17 (45.9%)	78 (56.5%)	0.251
Diabetes mellitus	16 (43.2%)	42 (30.4%)	0.142
Hypertension	19 (51.4%)	46 (33.31%)	0.044
Carotid stenosis	7 (18.9%)	20 (14.5%)	0.508
STEMI	28 (75.7%)	90 (65.2%)	0.228
NSTEMI	9 (24.3%)	48 (34.8%)	0.228
p-PCI	24 (64.9%)	61 (44.2%)	0.026

aABI = acute asymptomatic brain infarcts; BMI = body mass index; p-PCI = primary percutaneous coronary intervention; NSTEMI = non-ST segment elevation myocardial infarction; STEMI = ST-segment elevation myocardial infarction.

procedure and frequency of device insertion into the coronary artery. There were no significant differences in culprit lesion, contrast volume, stents per procedure, postprocedural TIMI-3 flow, activated coagulation time (ACT) after PCI and catheter experience, and use of aspiration devices. Results of multivariate analysis for statistical significant factors are reported in Table 5. Incidence of hypertension, proportion of p-PCI, Killip > 1 on admission, duration of procedure, and the frequency of device insertion into the coronary artery were reevaluated using logistic regression. Proportion of p-PCI , duration of procedure, and the frequency of device insertion into the coronary artery were indicated as independent factors related to the incidence of aABI, and others did not.

There were no differences in location of aABI between the right hemisphere 17 (46%) and the left hemisphere 20 (54%), anterior cerebral circulation 22 (59%) and posterior cerebral circulation 15 (41%) in our study.

4. Discussion

Stroke is a potential complication of PCI. Adjunctive antithrombotic medications during PCI may increase risk of intracranial hemorrhagic complications. The incidence of stroke was perhaps underestimated because of the occurrence of aABI, which could be easily ignored by clinicians because of the absence of symptoms or signs. With DW MRI, we analyzed the incidence of aABI after PCI. We found that patients with AMI without PCI did not have aABI lesions and the incidence of aABI reached 21.14% in patients with AMI and PCI through TRI.

Table 2
Laboratory data on admission.

	aABI group	Non-aABI group	*p*
	$n = 37$	$n = 138$	
WBC count ($\times 10^9$/L)	12.4 ± 3.7	11.5 ± 3.4	0.162
Total cholesterol (mg/dL)	195.4 ± 54.1	197.4 ± 48.5	0.828
Triglyceride (mg/dL)	175.2 ± 120.6	177.1 ± 130.7	0.936
HDL-cholesterol (mg/dL)	45.1 ± 10.1	43.5 ± 10.2	0.397
LDL-cholesterol (mg/dL)	124.3 ± 39.1	129.7 ± 40.2	0.467
Hs-CRP (mg/dL)	4.5 ± 3.6	3.8 ± 2.4	0.264
Blood sugar (mg/dL)	206 ± 78.5	192 ± 72.1	0.305
D-Dimer	1.5 ± 1.2	1.2 ± 0.7	0.142
CK-MB mass (ng/mL)	13.4 ± 28.9	23.1 ± 55.4	0.306
BNP (pg/mL)	215.2 ± 104.5	203.1 ± 101.3	0.522
Serum creatinine	1.0 ± 0.9	1.1 ± 1.0	0.582

aABI = acute asymptomatic brain infarcts; BNP = B-type natriuretic peptide: cut-off value of 100 pg/mL; CK-MB, creatine kinase isozyme MB; HDL = high-density lipoprotein; Hs-CRP = high-sensitivity C-reactive protein; LDL = low-density lipoprotein; WBC = white blood cell.

Table 3
Severity of acute myocardial infarction.

	aABI group	Non-aABI group	*p*
	$n = 37$	$n = 138$	
Peak of CK-MB mass (ng/mL)	214.8 ± 212.4	237.4 ± 208.1	0.560
Peak of cTnI mass (ng/mL)	31.5 ± 52.1	38.3 ± 58.5	0.522
Peak of BNP mass (pg/mL)	667.8 ± 315.4	645.4 ± 298.2	0.689
MBP on admission (mmHg)	100 ± 26	97 ± 24	0.508
Multivessel disease	15 (40.5%)	46 (33.3%)	0.414
Killip > 1 on admission	13 (35.1%)	26 (18.8%)	0.034
LVEF after admission (%)	54 ± 11	53 ± 8.1	0.605

aABI = acute asymptomatic brain infarcts; BNP = B-type natriuretic peptide: cut-off value of 100 pg/mL; CK-MB, creatine kinase isozyme MB; cTnI = cardiac troponin I; LVEF = left ventricular ejection fraction; MBP = mean blood pressure.

Table 4
Angiography characteristics and catheter procedure.

	aABI group	Non-aABI group	*p*
	$n = 37$	$n = 138$	
Culprit lesion			
LAD	12 (32.4%)	47 (34.1%)	0.853
LCX	5 (13.5%)	24 (17.4%)	0.573
RCA	20 (54.1%)	67 (48.5%)	0.552
Duration of procedure (min)	69.2 ± 27.3	57.4 ± 23.5	0.010
Contrast volume (mL)	180 ± 55	185 ± 65	0.669
Stents per procedure	1.5 ± 0.8	1.5 ± 1.0	0.999
Postprocedural TIMI-3 flow	34 (91.9%)	130 (94.2%)	0.894
ACT (s)	338 ± 82.5	324 ± 78.3	0.341
Frequency of device insertion	6.2 ± 3.1	5.0 ± 2.5	0.015
Aspiration device	16 (43.2%)	42 (30.4%)	0.142
Catheter experience ($n \geq 10$ y)	12 (32.4%)	41 (29.7%)	0.749

ACT = activated coagulation time; LAD = left anterior descending coronary artery; LCX = left circumflex coronary artery; RCA = right coronary artery.

Whether the approach to the coronary artery could affect the incidence of aABI during catheter procedures could not be fully proved. Murai et al[7] analyzed differences in the incidence of aABI after either the femoral artery or upper limb approach to the coronary artery during catheter procedures, and there were no differences ($p = 0.883$). Hamon et al[11] found a high incidence of silent cerebral infarct after cardiac catheterization of patients with aortic stenosis The risk of silent cerebral infarct did not differ significantly between the femoral and radial groups (incidence of 11.7% vs. 17.5%; odds ratio 0.85; 95% confidence interval, 0.62−1.16; $p = 0.31$)[11]. The influence of route of access on aABI has not been definitively established and additional research is needed.

Our research and previous studies[6,7] showed that without catheter manipulation no patients had aABI. It was suggested that aABI occurred because of manipulation of catheters. The size and shape of the lesion on DWI suggested that embolic stroke was the cause of aABI. An embolic source in patients undergoing PCI was not clear. There was no statistical difference in extracranial carotid artery stenosis between the aABI and non-aABI groups. Moreover, there was no catheter manipulation in the carotid arteries during cardiac catheterization, and there was strong indication that that

Table 5
Multivariate analysis for statistically significant factors.

	OR (95%CI)	*p*
Hypertension	2.11 (1.01−4.41)	0.108
p-PCI	2.33 (1.16−4.98)	0.035
Killip > 1 on admission	2.31 (1.01−5.04)	0.465
Duration of procedure	2.34 (1.23−5.28)	0.041
Frequency of device insertion	2.06 (1.24−4.92)	0.018

CI = confidence interval; OR = odds ratio; p-PCI = primary percutaneous coronary intervention.

carotid artery embolism was not an emboli source. All data strongly indicated that catheter manipulations were important sources. We found that the independent factors related to aABI following PCI were p-PCI, duration of procedure, and the frequency of device insertion into the coronary artery. However, other studies showed different results. Murai et al[7] found that PCI time was not an independent factor related to asymptomatic acute ischemic stroke. Most reports currently indicate that procedural time was an independent predictor of the occurrence of cerebral infarction[6,12,13]. Murai et al[7] reported that the independent factors related to asymptomatic acute ischemic stroke following p-PCI were right coronary artery (RCA) as the culprit vessel and the frequency of device insertion into the coronary artery. We also found that the frequency of device insertion into the coronary artery was an independent predictor of the occurrence of aABI, but we did not find that RCA as the culprit vessel was an independent predictor. These results suggested that aABI mainly occurs either while manipulating the catheter or device at the bottom of the ascending aorta, which scratches the aortic wall[14], when pulling a thrombus through the coronary artery using devices, or when pushing air bubbles out of the guiding catheters while using devices or contrast medium[15,16]. However, currently there is no evidence to define the source of emboli.

We found that the incidence of aABI in patients who underwent p-PCI and those who underwent e-PCI was significantly different (28.2% vs. 14.4%, $p = 0.026$) and p-PCI was an independent predictor of the occurrence of aABI. The strong association with p-PCI in multivariate analysis was noteworthy and has not been reported previously. The mechanism is not clear. Some possible reasons include embolism because of high coagulability, and distal emboli of fragile plaque from the coronary ostial lesion, in particular when thrombus aspiration devices are used[7]. However, as in previous studies, we also could not find a statistical difference between the aABI and non-aABI groups in the frequency of using thrombus aspiration devices because patient numbers were small. Further investigations are required to explain the mechanism.

There were no differences in location of aABI between right hemisphere and left hemisphere, anterior cerebral circulation, and posterior cerebral circulation in our study. We can see that all lesions were either located in noneloquent brain areas or were too small to be clinically apparent. The long-term effect of such lesions has not been investigated, but there are indications that they may lead to impaired cognitive function[17–19]. aABI has been associated with dementia or depression. Fujikawa et al identified silent brain ischemia on MRI in 51.4% of patients with presenile-onset presenile depression, in 65.9% of those with presenile-onset senile depression, and in 93.7% of those with senile-onset depression[20]. In addition, Vermeer et al concluded from a mean 3.6-year follow-up of 1015 participants that the presence of silent brain ischemia at baseline more than doubled the risk of dementia[21]. The relationship between aABI and dementia or depression is not clear and should be investigated in the future.

5. Study limitations

The current study has certain limitations; there were relatively few patients and the number of those with aABI was small. Another limitation is that cranial MRI was not performed before PCI for ethical reasons. Hence, the results of the current study should be interpreted with caution.

6. Conclusion

Cranial MRI following PCI revealed that 21.14% of the patients with AMI had aABI. The independent factors related to aABI following PCI were p-PCI, duration of procedure, and the frequency of device insertion into the coronary artery.

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